

II. REMARKS

Applicant amends claims 27, 29, 32 and 34-39 to correct typographical errors and provide proper antecedent basis for the claims. No new matter has been added.

AMENDMENTS TO THE CLAIMS

1. (Previously Presented) An isolated antibody or antibody fragment thereof which comprises an antigen-binding domain of a human antibody specific for human TGF β .
2. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 which is in the form of scFv.
3. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 which is in the form of a whole antibody.
4. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises part or all of a VH domain encoded by a germ line gene segment or a rearranged gene segment.
5. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises part or all of either a VL kappa domain or a VL lambda domain.
6. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VH domain consisting of the amino acid sequence as shown in any one of Fig. 1(a)(i) to (iv) (SEQ ID NOS: 8, 111, 112 and 10) or Fig. 1(c)(i) (SEQ ID NO: 12).
7. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain consisting of the amino acid

sequence as shown in any one of Fig. 1(a)(v) (SEQ ID NO: 14) or Fig. 1(b) (SEQ ID NOS: 16 and 18).

8. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VH domain consisting of the amino acid sequence as shown in any one of Fig. 2(a)(i) to (iii) (SEQ ID NOS: 6, 37 and 116), (v) (SEQ ID NO: 120), and (vi) (SEQ ID NO: 122).

9. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain consisting of the amino acid sequence as shown in any one of Fig. 2(a)(iv) (SEQ ID NO: 118) or Fig. 2(b)(i) to (vi) (SEQ ID NOS: 39, 41, 43, 45, 47, 124).

10. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain consisting of the amino acid sequence as shown in Fig. 4 (SEQ ID NO: 49).

11. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain encoded by the nucleotide sequence as shown in Fig. 4 (SEQ ID NO: 48).

12. (Previously Presented) A polypeptide with a binding domain specific for TGF β which polypeptide comprises an amino acid sequence as shown in any one of Fig. 1(a) (SEQ ID NOS: 8, 111, 112, 10, 14), Fig. 1(b) (SEQ ID NOS: 16 and 18), Fig. 1(c) (SEQ ID NO: 12), Fig. 2(a)

(SEQ ID NOS: 6, 37, 116, 118, 120 and 122), Fig. 2(b) (SEQ ID NOS: 39, 41, 43, 45, 47, 124), and Fig. 4 (SEQ ID NO: 49).

13. (Previously Presented) An isolated antibody or antibody fragment thereof comprising an antigen-binding domain of a human antibody specific for human TGF- β , said antigen-binding domain comprising the VH domain 6H1 VH of which the amino acid sequence is shown in Figure 2(a)(i) (SEQ ID NO: 6).

14. (Previously Presented) An antibody or antibody fragment thereof according to claim 13 which is in the form of scFv.

15. (Previously Presented) An antibody or antibody fragment thereof according to claim 13 which is in the form of a whole antibody.

16. (Previously Presented) An antibody or antibody fragment thereof according to claim 13 wherein said antigen-binding domain of a human antibody comprises a VL domain selected from 6B1 VL, of which the amino acid sequence is shown in Figure 2(b)(iii) (SEQ ID NO: 43), 6H1 VL, of which the amino acid sequence is shown in Figure 2(b) (vi) (SEQ ID NO: 124), and 6A5 VL, of which the amino acid sequence is shown in Figure 2(b)(ii) (SEQ ID NO: 41).

17. (Previously Presented) An antibody or antibody fragment thereof according to claim 16 which is in the form of scFv.

18. (Previously Presented) An antibody or antibody fragment thereof according to claim 16 which is in the form of a whole antibody.

19. (Previously Presented) An isolated antibody or antibody fragment thereof comprising an antigen-binding domain of a human antibody specific for human TGF β , said antigen-binding domain of a human antibody comprising the VH domain 6H1 VH of which the amino acid sequence is shown in Figure 2(a)(i) (SEQ ID NO: 6) and the VL domain 6B1 VL, of which the amino acid sequence is shown in Figure 2(b)(iii) (SEQ ID NO: 43).

20. (Previously Presented) An antibody or antibody fragment thereof according to claim 19 which is in the form of scFv.

21. (Previously Presented) An antibody or antibody fragment thereof according to claim 19 which is in the form of a whole antibody.

22. (Previously Presented) A composition which comprises an antibody or antibody fragment thereof, according to claim 13 and an excipient.

23. (Previously Presented) A composition which comprises an antibody or antibody fragment thereof, according to claim 19 and an excipient.

24. (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, wherein said human antibody antigen binding domain comprises a VH domain which has the amino acid sequence shown in Figure 1 (a) (i) (SEQ ID NO: 8).

25. (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially

over TGF β 3 and which neutralizes TGF β 1, wherein said human antigen binding domain comprises a VL domain which has the amino acid sequence shown in Figure 14 (SEQ ID NO: 59).

26. (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, wherein said human antibody antigen binding domain comprises a pairing of a VH domain and a VL domain selected from:

- (a) 1B2 VH, of which the amino acid sequence is shown in Figure 1 (a) (i) (SEQ ID NO: 8), and 7A3 VL, of which the amino acid sequence is shown in Figure 1 (b) (i) (SEQ ID NO: 16);
- (b) 31G9 VH, of which the amino acid sequence is shown in Figure 1 (a) (iv) (SEQ ID NO: 10), and 31G9 VL, of which the amino acid sequence is shown in Figure 1 (a) (v) (SEQ ID NO: 14); and
- (c) 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ ID NO: 12), and 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

27. (Currently Amended) A specific binding member according to claim [[18]] **26** wherein said human antibody antigen binding domain comprises a VH domain 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ ID NO: 12), and the VL domain 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

28. (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, wherein said human antibody antigen binding domain comprises a VH domain which comprises a CDR3 with an amino acid sequence selected from those shown in Figure 3 (SEQ ID NOS: 19-35).

29. (Currently Amended) A specific binding member according to claim ~~[[20]]~~ **28** wherein said CDR3 has the sequence shown for CDR3 of 27C1 VH (SEQ ID NO: 12). (BUT NO ANTECEDENT BASIS FOR SEQ ID NO:12)

30. (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, wherein said human antibody antigen binding domain comprises the 31 G9 VH domain of which the amino acid sequences is shown in Figure 1 (a) (iv) (SEQ ID NO: 10) and the CS37 VL of which the sequence is shown in Figure 14 (SEQ ID NO: 59).

31. (Previously Presented) A specific binding member which is a first specific binding member comprising a first human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, wherein said first specific binding member competes for binding to TGF β 1 with a second specific binding member comprising a second human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, wherein said second human antibody antigen binding domain comprises a pairing of a VH domain and a VL domain selected from:

- (a) 1 B2 VH, of which the amino acid sequence is shown in Figure 1 (a) (i) (SEQ ID NO: 8), and 7A3 VL, of which the amino acid sequence is shown in Figure 1 (b) (i) (SEQ ID NO: 16);
- (b) 31G9 VH, of which the amino acid sequence is shown in Figure 1(a) (iv) (SEQ ID NO: 10), and 31G9 VL, of which the amino acid sequence is shown in Figure 1 (a) (v) (SEQ ID NO: 14); and
- (c) 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ

ID NO: 12), and the VL domain 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

32. (Currently amended) A first specific binding member according to claim ~~[[23]]~~ **31**, wherein said second human antibody antigen binding domain comprises the VH domain 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ ID NO: 12), and the VL domain 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

33. (Previously Presented) A specific binding member which is a first specific binding member comprising a first human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, and wherein said first specific binding member competes for binding to TGF β 1 with a second specific binding member comprising a second human antibody antigen binding domain specific for human TGF β isoform TGF β 1 which binds TGF β 1 preferentially over TGF β 3 and which neutralizes TGF β 1, and wherein said second human antibody antigen binding domain comprises the 31 G9 VH domain of which the sequence is shown in Figure 1 (a) (iv) (SEQ ID NO: 10) and the CS37 VL of which the sequence is shown in Figure 14 (SEQ ID NO: 59).

34. (Currently Amended) A specific binding member as in any one of claims ~~16, 17, 18, 20, 22, 23, or 25~~ **24, 25, 26, 28, 30, 31 or 33** comprising a single-chain Fv antibody molecule.

35. (Currently Amended) A specific binding member as in any one of claims ~~16, 17, 18, 20, 22, 23, or 25~~ **24, 25, 26, 28, 30, 31 or 33** which comprises one or more amino acids in addition to those forming said human antibody antigen binding domain.

- 36.** (Currently Amended) A specific binding member according to claim ~~[[31]]~~ **35** comprising an antibody constant region.
- 37.** (Currently Amended) A specific binding member according to claim ~~[[32]]~~ **36** which comprises a whole antibody.
- 38.** (Currently Amended) A specific binding member according to claim ~~[[32]]~~ **36** wherein said antibody constant region is IgG4 isotype.
- 39.** (Currently Amended) A pharmaceutical composition comprising a specific binding member as in any one of claims ~~16, 17, 18, 20, 22, 23, or 25~~ **24, 25, 26, 28, 30, 31 or 33** and a pharmaceutically acceptable excipient.

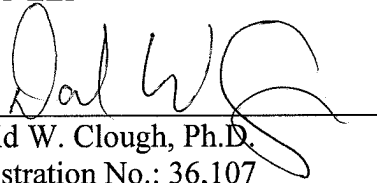
CONCLUSION

The Examiner is hereby respectfully invited to contact the undersigned attorney at the number listed below with any questions, comments or suggestions relating to this application.

Respectfully submitted,

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